

## **REMARKS**

Claims 43, 46-48, 50, 52-55 are pending in this application. Method claims 23, 25-42 are canceled above, without prejudice or disclaimer, to simplify this application; Claim 45 is canceled because it has a typographical error, again to simplify this application. Applicants reserve the right to present any of these canceled claims in another application, such as a continuation application.

### **Obviousness Rejections**

At page 3 of the office action, Claims 23, 26-28, 30-35, 37-44, 46-48, 50, and 53-55 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Mechoulam or Volicer, in view of McNally.<sup>1</sup>

At page 4 of the office action, Claims 43-48, 50, and 52-55 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Pars in view of McNally.

Applicants respectfully traverse the obviousness rejections.

Applicant's independent claim 43 recites: "A pharmaceutical composition comprising a hydrofluoroalkane,  $\Delta^9$ -tetrahydrocannabinol, and up to 15 percent by weight of an organic solvent, said  $\Delta^9$ -tetrahydrocannabinol and said organic solvent being dissolved in said hydrofluoroalkane to form a stable composition, wherein said  $\Delta^9$ -tetrahydrocannabinol is present in said composition in concentrations ranging from 0.147% w/w ( $\pm 0.008$ ) to 5.940% w/w ( $\pm 0.191$ )."

Mechoulam fails to disclose the pharmaceutical composition of Applicant's claim 43, for at least the reasons that: Mechoulam fails to teach hydrofluoroalkane (HFA) as recited in Applicant's claim 43. Mechoulam fails to teach  $\Delta^9$ -tetrahydrocannabinol and an organic solvent being dissolved in hydrofluoroalkane to form a stable composition as recited in Applicant's claim 43. The Examiner incorrectly treats these differences as de minimis.

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<sup>1</sup>At page 3 of the office action, dependent Claim 36 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Mechoulam, Volicer, McNally, and the 1997 "Appetite Stimulation" reference. At page 3 of the office action, dependent Claims 25, 45, and 52 have been rejected over Mechoulam or Volicer combined with McNally, further in view of Pars. At page 4 of the office action, Claim 29 has been rejected over Mechoulam or Volier combined with McNally, and Ohlsson.

**Unexpectedly Superiority of Applicants' Claimed Invention: Aerosolizability**

The pharmaceutical compositions claimed by Applicants are substantially and patentably different from Mechoulam. None of the actual prepared examples in Mechoulam is an aerosol but rather the drugs were administered orally in the Mechoulam examples (col. 11, line 42). Other than Applicant's work of record herein, there is no evidence of any previous person actually constructing a pharmaceutical composition comprising any form of THC wherein the pharmaceutical composition was aerosolized. The unrebutted evidence of record is that "Despite the fact that the interest in THC dates back nearly thirty years ..., no acceptable delivery systems of inhalation THC have been developed." (Dr. Weers' Declaration, sentence bridging pages 8-9.) Mechoulam's actual examples are non-aerosol.

By contrast, the evidence of record in Applicants' specification and the 1.132 Declaration of Dr. Weers establishes that a representative example of Applicants' claim 43 is aerosolizable. Aerosol delivery is a superior, highly desirable delivery mode for THC.<sup>2</sup> Thus representative examples of Applicant's claim 43 are unexpectedly superior to the non-aerosol actual examples of Mechoulam. The unexpected superiority of representative embodiments of Applicant's claim 43 over the actual examples in the primary reference Mechoulam requires the Examiner to recognize that the *prima facie* case of obviousness has been rebutted. As MPEP 716.02(a) states, in the section "Presence of an unexpected property is evidence of nonobviousness": "Presence of a property not possessed by the prior art is evidence of nonobviousness."

Likewise, Applicant's independent claim 50 is not obvious over Mechoulam.

The Examiner also has cited Volicer as a primary reference. Volicer is substantially distinguished from Applicant's claim 43 for at least the following reasons: Volicer fails to disclose hydrofluoroalkane used with  $\Delta^9$ -tetrahydrocannabinol as recited in Applicant's claim 43. Volicer fails to disclose  $\Delta^9$ -tetrahydrocannabinol and an organic solvent dissolved in hydrofluoroalkane to form a stable composition.

In the actual examples in Volicer, the dronabinol<sup>3</sup> was in capsule form. (Col. 7, line 25.)

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<sup>2</sup>See Dr. Weers' Declaration, page 8: "the pharmacokinetics of tetrahydrocannabinol following inhalation is considerably more favorable than the oral route of administration."

<sup>3</sup>The undisputed evidence of record is that dronabinol undergoes extensive first-pass hepatic metabolism resulting in only 10-20% of the administered dose reaching system

Again, a representative embodiment of Applicants' claimed invention provides unexpectedly superior results compared to the Volicer examples which were non-aerosols.

Turning to the obviousness rejection in which Pars is cited as the primary reference, Applicants note that none of the Pars examples are aerosols. As has been stated above, representative embodiments of Applicants' claimed invention of pharmaceutical compositions provide the unexpectedly superior result of aerosolizability compared to representative embodiments of Pars which are non-aerosols.

Reconsideration and withdrawal of the obviousness rejections are respectfully requested.

For simplicity and brevity, Applicants do not respond to each comment by the Examiner regarding Dr. Weers' Declaration at pages 6-12 of the office action. This is not because Applicants agree with the comments,<sup>4</sup> but because it is believed to be simpler and more constructive to communicate about the fact that no primary reference (Mechoulam, Volicer, Pars), or indeed no reference at all, discloses an actual example of aerosolized THC. None before Applicants provided a THC-comprising pharmaceutical composition such as Applicants' claimed composition that had the highly desirable -- but elusive -- characteristic of being aerosolizable.

**Non-combinability of primary and secondary references due to structural differences**

The *prima facie* case of obviousness is further and additionally destroyed by the non-combinability of any of the primary references with any of the secondary references, for the reason that the chemical structure of THC (in the primary references) differs from the chemical structures of the substances in the secondary references so that the secondary references should be withdrawn. The final office action sets forth a chemical structure for THC (recited in Applicants' claims and

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circulation. (Dr. Weers' Declaration, sentence bridging pages 7-8.) Therefore dronabinol is quite inferior to Applicant's claimed pharmaceutical composition which can be aerosolized resulting in much more reaching system circulation.

<sup>4</sup>For example, at page 5 of the office action, the Examiner's first comment about Dr. Weers' Declaration is to comment, incorrectly, that Dr. Weers' declaration at "Paragraph 1/section ... fails to indicate what is the relationship both past and present between Dr. Weers and the inventors/assignee of the instant application." To the contrary, the first sentence of the Declaration, page 1, paragraph 1, states that Dr. Weers is "currently employed by Nektar Therapeutics" which was previously known by another name and "which has licensed the above-identified patent application".

disclosed in the primary references. McNally is cited as a secondary reference, for teaching butixocort. The Examiner (at page 7 of the final office action) criticizes Dr. Weers in his Declaration for discussing butixocort as having a drastically different chemical structure from THC, but the reason Dr. Weers was discussing butixocort in the first instance was because butixocort was relied-upon and discussed by the Examiner in his citation of the McNally secondary reference (e.g., Office Action dated December 28, 2005, page 6.) The butixocort-related McNally reference should be withdrawn for its non-combinability with any of the THC-related primary references.

**Non-statutory Double Patenting**

At page 5 of the office action, Claims 26-29, 43, 44, 46, 48, 50, and 52-55 have been rejected for nonstatutory obviousness-type double patenting based on claims 1-12 of U.S. Patent No. 6,509,005.

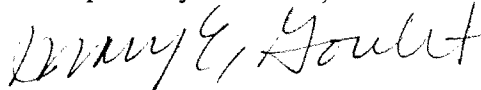
As has been stated before, this issue will be addressed in due course by filing a Terminal Disclaimer.

In view of the foregoing, it is respectfully requested that the application be reconsidered, that claims 43, 46-48, 50, 52-55 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at the local telephone number listed below to discuss any other changes deemed necessary in a telephone or personal interview.

A provisional petition is hereby made for any extension of time necessary for the continued pendency during the life of this application. Please charge any fees for such provisional petition and any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,



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